

Breast Cancer Prevention Studies

Key Points

- Breast cancer prevention studies are clinical trials involving women who have not had cancer, but are at high risk of developing the disease.
- In the Breast Cancer Prevention Trial (BCPT), the women who received tamoxifen had a lower incidence of breast cancer than the women who did not receive the drug. Results of this study were published in 1998 (see Breast Cancer Prevention Trial (BCPT) section).
- Another trial, the Study of Tamoxifen and Raloxifene (STAR), is comparing raloxifene with tamoxifen. Results of this study are expected in 2006 (see Study of Tamoxifen and Raloxifene (STAR) section).
- The Capital Area SERM Study is testing raloxifene in premenopausal women who are at high risk for breast cancer. A complete report of the findings will be published early in 2005 (see Capital Area SERM Study section).
- Other breast cancer prevention studies are in progress (see Other Breast Cancer Prevention Studies section).

Breast cancer prevention studies are clinical trials (research studies conducted with people) that explore ways of reducing the risk, or chance, of developing breast cancer.

Prevention studies usually involve women who have not had breast cancer, but are at high risk of developing the disease. Through such studies, scientists hope to determine what steps are effective in reducing the risk of breast cancer in women of all races and ethnic backgrounds.

Most breast cancer prevention research is based on evidence linking the development of this disease, in many cases, with exposure to the hormone estrogen. The focus of several recent



breast cancer prevention studies has been on testing the effectiveness of drugs called selective estrogen receptor modulators (SERMs). SERMs are drugs that have some anti-estrogen properties and some estrogen-like properties. Their anti-estrogen activity may help reduce the risk of breast cancer by blocking the effects of estrogen on breast tissue. Their estrogen-like properties may help prevent the loss of bone density in postmenopausal women; however, SERMs may cause bone loss in premenopausal women.

The Breast Cancer Prevention Trial (BCPT)

The Breast Cancer Prevention Trial (BCPT) was funded by the National Cancer Institute (NCI) and conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP). The BCPT was designed to see whether tamoxifen (Nolvadex®), a SERM, can prevent breast cancer in women who are at an increased risk of developing this disease. The study began recruiting participants in April 1992 and closed enrollment in September 1997. This study involved 13,388 premenopausal and postmenopausal women at more than 300 centers across the United States and Canada.

Results showed 49 percent fewer diagnoses of invasive breast cancer in women who were randomized to take tamoxifen compared with women who were randomized to take a placebo (an inactive substance that looks the same as, and is administered in the same way as, a drug in a clinical trial). Women on tamoxifen also had 49 percent fewer diagnoses of noninvasive breast tumors, such as ductal or lobular carcinoma in situ. Nine women died of breast cancer, three women in the tamoxifen group and six women in the placebo group (1).

In the BCPT, most of the side effects associated with tamoxifen were temporary. However, there were some long-term risks, including several serious health problems:

endometrial cancer (cancer of the lining of the uterus), uterine sarcoma (cancer of the muscular wall of the uterus), pulmonary embolism (blood clot in the lung), deep vein thrombosis (blood clot in a large vein), and stroke. Because of these risks, women taking tamoxifen should be monitored by their doctors for any sign of serious side effects. All BCPT participants have been asked to undergo regular follow-up examinations.

BCPT participants who were randomized to the tamoxifen group and had not completed 5 years of tamoxifen therapy when the study ended were given the opportunity to continue on therapy. Postmenopausal women who had been taking the placebo were invited to participate in another trial, the Study of Tamoxifen and Raloxifene (STAR). (See the following section for a description of this trial.) Women in the BCPT placebo group also have the option of seeking tamoxifen from their doctor.

The Study of Tamoxifen and Raloxifene (STAR)

The NSABP is conducting the Study of Tamoxifen and Raloxifene, known as STAR. The study is funded primarily by the NCI. The 19,000 participants are postmenopausal women who are at least 35 years old and are at increased risk for developing breast cancer. The study will determine how raloxifene (Evista®), another SERM, compares with tamoxifen in reducing the incidence of breast cancer in women who are at an increased risk of developing the disease. As with tamoxifen, most of the known side effects of raloxifene are temporary. However, like tamoxifen, raloxifene increases the risk of pulmonary embolism and deep vein thrombosis. STAR is closed to new participants, and results are expected in the summer of 2006.

Capital Area SERM Study

The NCI is also conducting the Capital Area SERM Study to evaluate the safety of raloxifene in premenopausal women between the ages of 23 and 47 who are at increased risk for breast cancer. Thirty-seven women enrolled in this study. A complete report of the study's findings will be published in 2005.

Other Breast Cancer Prevention Studies

Drugs called aromatase inhibitors, which have been approved by the U.S. Food and Drug Administration to treat hormone-sensitive breast cancer, are being studied in clinical trials for breast cancer prevention. These drugs interfere with the adrenal enzyme aromatase, which is responsible for estrogen production in postmenopausal women (2). The NCI is also studying prevention options for women at high risk of breast cancer that is not sensitive to hormones and can be more difficult to treat than hormone-sensitive breast cancer. More information about these and other clinical trials is available from the NCI's Cancer Information Service (CIS) at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI's Web site at <http://www.cancer.gov> on the Internet.

Scientists are also studying the basic biology of breast cancer to learn more about both non-hormone-sensitive and hormone-sensitive tumors. This research may lead to better ways of preventing all types of breast cancer.

NCI Priorities for Breast Cancer Prevention Research

Recognizing the impact of breast cancer on our society, in 1997 the NCI convened a Breast Cancer Progress Review Group (PRG) of experts and advocates to analyze the NCI's

breast cancer research activities and develop recommendations for the future. Based on its assessment of the status of breast cancer research, the review group recommended research priorities to accelerate progress in breast cancer prevention and treatment. In August 1998, the group published its report, *Charting the Course: Priorities for Breast Cancer Research*. This report is available at <http://prg.nci.nih.gov/breast/finalreport.html> on the Internet.

In October 2004, an internal NCI Breast Cancer Working Group assessed the advances made since the release of the PRG report. The Working Group released *The NCI Breast Cancer Progress Report*, which documents trends in NCI's breast cancer research portfolio and the progress that has been made in meeting the priorities identified by the PRG. The report will help to guide the Institute as it moves forward in breast cancer research. This report is available at <http://prg.nci.nih.gov/breast/progress.html> on the Internet.

Estimating Breast Cancer Risk

Most breast cancer prevention trials involve women at increased risk of developing this disease. For example, it is clear that breast cancer occurs more often in women over age 60. Other factors associated with increased risk include a personal or family history of breast cancer and changes in certain genes such as BRCA1 and BRCA2. Scientists at the NCI and the NSABP have developed a computer program (on CD-ROM) called the Breast Cancer Risk Assessment Tool. This tool can help women and their health care providers estimate a woman's chances of developing breast cancer based on several recognized risk factors. The Breast Cancer Risk Assessment Tool also provides information on tamoxifen. A copy of the CD may be ordered by calling the NCI's CIS at 1-800-4-CANCER (1-800-422-6237), or from the NCI Publications Locator at <http://www.cancer.gov/publications> on the NCI's Web site.

Options for Women at Increased Risk

Doctors generally suggest that high-risk women be closely monitored and have regular medical checkups so that, if breast cancer develops, it is likely to be detected at an early stage (3). These women may also consider participating in prevention studies, taking tamoxifen, or undergoing preventive surgery to reduce breast cancer risk. Preventive mastectomy is surgery to remove one or both breasts in an effort to prevent or reduce the risk of breast cancer (4). Existing data suggest that preventive mastectomy may significantly reduce (by about 90 percent) the chance of developing breast cancer in moderate- and high-risk women (5). Other data suggest that preventive oophorectomy (surgery to remove the ovaries of women at high risk of ovarian cancer because of BRCA1 or BRCA2 gene mutations) may reduce the risk of breast cancer by about 50 percent (6).

The decision to join a study, take tamoxifen, or undergo preventive surgery is an individual one. With any medical procedure or intervention, both the benefits and the risks of the therapy must be considered. The balance of these factors will vary depending on a woman's personal and family health history and how she weighs the benefits and risks. Women who are considering surgery or other steps to reduce the risk of breast cancer should discuss their personal risk factors with their doctor.

Selected References

1. Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for prevention of breast cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. *Journal of the National Cancer Institute* 1998; 90(18):1371–1388.
2. Chlebowski RT, Col N, Winer EP, et al. American Society of Clinical Oncology technology assessment of pharmacologic interventions for breast cancer risk reduction including tamoxifen, raloxifene, and aromatase inhibition. *Journal of Clinical Oncology* 2002; 20(15):3328–3343.

3. Thull DL, Vogel VG. Recognition and management of hereditary breast cancer syndromes. *The Oncologist* 2004; 9(1):13–24.
4. Stefanek M, Hartmann L, Nelson W. Risk-reduction mastectomy: Clinical issues and research needs. *Journal of the National Cancer Institute* 2001; 93(17):1297–1306.
5. Hartmann LC, Schaid DJ, Woods JE, et al. Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. *New England Journal of Medicine* 1999; 340(2):77–84.
6. Rebbeck TR, Lynch HT, Neuhausen SL, et al. Prophylactic oophorectomy in carriers of BRCA1 or BRCA2 mutations. *New England Journal of Medicine* 2002; 346(21): 1616–1622.

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Related Resources

Publications (available at <http://www.cancer.gov/publications>)

- National Cancer Institute Fact Sheet 4.19, *The Study of Tamoxifen and Raloxifene (STAR): Questions and Answers*
- National Cancer Institute Fact Sheet 7.5, *Preventive Mastectomy: Questions and Answers*
- National Cancer Institute Fact Sheet 7.16, *Tamoxifen: Questions and Answers*
- *Taking Part in Clinical Trials: Cancer Prevention Studies: What Participants Need To Know*
- *What You Need To Know About™ Breast Cancer*

National Cancer Institute (NCI) Resources

Cancer Information Service (toll-free)

Telephone: 1-800-4-CANCER (1-800-422-6237)

TTY: 1-800-332-8615

Online

NCI's Web site: <http://www.cancer.gov>

LiveHelp, NCI's live online assistance:

<https://cissecure.nci.nih.gov/livehelp/welcome.asp>

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